

Please amend the application as follows:

AMENDMENTS

Please amend currently pending claims 63, 71, 75, 79, 81, 89, 90, 94 and 102, and add new claims 110 to 123 as below.

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C1
63. (Amended) A method of identifying a G-protein coupled receptor (GPCR) for a given ligand, the method comprising:

- (i) expressing a putative GPCR in a cell, said cell comprising,
 - a) a first heterologous promoter operably linked to a first polynucleotide encoding a Gα15 protein having at least 70 % sequence homology to SEQ. ID. NO. 2,
 - b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene,

wherein said cell stably expresses said Gα15 protein at sufficient levels to permit promiscuous coupling to said GPCR, and

wherein said second heterologous promoter is directly or indirectly modulated by the activity of said Gα15 protein,

- (ii) contacting said cell with said ligand; and
- (iii) detecting a change in reporter gene expression by comparing reporter gene expression prior to addition of said ligand with reporter gene expression after addition of said ligand.

64. The method of claim 63 wherein said cell comprises a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR.

65. The method of claim 63, wherein said GPCR is not naturally expressed in said cell.

Sub 31 66. The method of claim 63, wherein said GPCR is a taste receptor.

Sub 32 67. The method of claim 66, further comprising contacting said cell with a reporter gene substrate.

Sub 33 68. The method of claim 63, further comprising contacting said cell with a compound that increases calcium levels inside said cell.

69. The method of claim 68, wherein said compound is selected from the group consisting of ionomycin and thapsigargin.

70. The method of claim 68, further comprising contacting said cell with phorbol myristate acetate or an analog thereof.

Sub 03
Sub 34
C2 71. (Amended) A method for identifying a GPCR for a given ligand, the method comprising:

- i) expressing a putative GPCR in a cell, said cell comprising, a first heterologous promoter operably linked to a first polynucleotide encoding a $G\alpha_{15}$ protein having at least 70 % sequence homology to SEQ. ID. NO. 2,
wherein said cell stably expresses said $G\alpha_{15}$ protein at sufficient levels to permit promiscuous coupling to said GPCR and wherein said GPCR is normally coupled to either $G\alpha_i$, $G\alpha_s$ or $G\alpha_{12}$ in the absence of said $G\alpha_{15}$ protein;
- ii) contacting said cell with said ligand; and
- iii) detecting a change in a signal with a signal transduction detection system by comparing said signal prior to addition of said ligand with said signal after addition of said ligand,
wherein said signal transduction detection system comprises a dye.

72. The method of claim 71 wherein said cell comprises a second heterologous promoter operably linked to a second polynucleotide encoding said GPCR.

73. The method of claim 71, wherein said GPCR is not naturally expressed in said cell.

74. The method of claim 71, wherein said signal transduction detection system comprises an intracellular calcium indicator.

75. (Amended) A method of identifying of a ligand for a GPCR, the method comprising:

- i) contacting a cell with a test chemical, said cell comprising a first heterologous promoter operably linked to a first polynucleotide encoding a $G\alpha_{15}$ protein having at least 70 % sequence homology to SEQ. ID. NO. 2, wherein said cell stably expresses said $G\alpha_{15}$ protein at sufficient levels to permit promiscuous coupling to said GPCR and wherein said GPCR is normally coupled to either $G\alpha_i$, $G\alpha_s$ or $G\alpha_{12}$ in the absence of said $G\alpha_{15}$ protein;
- ii) detecting a change in a signal with a signal transduction detection system by comparing said signal prior to addition of said test chemical with said signal after addition of said test chemical, wherein said signal transduction detection system comprises a dye.

76. The method of claim 75 wherein said cell further comprises a second heterologous promoter operably linked to a second polynucleotide encoding a GPCR.

77. The method of claim 76 wherein said GPCR is not naturally expressed in said cell.

Sub 35
78. The method of claim 75, wherein said signal transduction detection system comprises an intracellular calcium indicator.

Sub 35
79. (Amended) The method of claim 75, further comprising comparing a signal from a first plurality of cells in the presence of said test chemical with either:
i) a signal from a second plurality of cells in the presence of said test chemical, wherein said second plurality of cells lack either a promiscuous G α protein, a target protein, or
ii) a signal from said first plurality of cells in the absence of said test chemical.
C4

Sub 36
80. The method of claim 75, wherein said detecting comprises fluorescence detection.

Sub 36
81. (Amended) A method of identifying a ligand for a GPCR, the method comprising
i) contacting a cell with a test chemical, said cell comprising,
a) a first heterologous promoter operably linked to a first polynucleotide encoding a G α 15 protein having at least 70 % sequence homology to SEQ. ID. NO. 2,
b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene,
wherein said cell stably expresses said G α 15 protein at sufficient levels to permit promiscuous coupling to said GPCR,
and
wherein said second heterologous promoter is directly or indirectly modulated by the activity of said G α 15 protein;
ii) detecting a change in reporter gene expression by comparing reporter gene expression prior to addition of said ligand with reporter gene expression after addition of said ligand.
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82. The method of claim 81 wherein said cell comprises a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR.

83. The method of claim 81, wherein said GPCR is not naturally expressed in said cell.

Sub 37
84. The method of claim 81, wherein said detecting comprises fluorescence detection.

Sub 07
85. The method of claim 81, further comprising contacting said cell with a reporter gene substrate.

Sub 34
86. The method of claim 81, further comprising contacting said cell with a compound that increases calcium levels inside said cell.

87. The method of claim 86, wherein said compound is selected from the group consisting of ionomycin and thapsigargin.

88. The method of claim 81, further comprising contacting said cell with phorbol myristate acetate or an analog thereof.

Sub 02
89. (Amended) The method of claim 81, further comprising comparing a signal from a first plurality of cells in the presence of said test chemical with either:

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- i) a signal from a second plurality of cells in the presence of said test chemical, wherein said second plurality of cells lack either a promiscuous G α protein, a target protein, or
 - ii) a signal from said first plurality of cells in the absence of said test chemical.

90. (Amended) A method for identifying a modulator of signal transduction in a cell, the method comprising:

- 66*
Correct but 08
- a) contacting a cell with a test chemical, said cell comprising a first heterologous promoter operably linked to a first polynucleotide encoding a Gα15 protein having at least 70 % sequence homology to SEQ. ID. NO. 2, wherein said cell stably expresses said Gα15 protein at sufficient levels to permit promiscuous coupling to said GPCR and wherein said GPCR is normally coupled to either Gα_i, Gα_s or Gα₁₂ in the absence of said Gα15 protein;
- b) contacting said cell with a ligand that, in the absence of the test chemical, activates signal transduction in said cell, and
- c) detecting a change in a signal with a signal transduction detection system by comparing said signal prior to addition of said test chemical with said signal after addition of said test chemical.

91. The method of claim 90 wherein said cell further comprises a second heterologous promoter operably linked to a second polynucleotide encoding a GPCR.

92. The method of claim 90, wherein said GPCR is not naturally expressed in said cell.

See 910

93. The method of claim 90, wherein said signal transduction detection system comprises an intracellular calcium indicator.

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94. (Amended) A method for identifying a modulator of signal transduction in a cell, the method comprising:

- i) contacting a cell with a test chemical, said cell comprising,
- a) a first heterologous promoter operably linked to a first polynucleotide encoding a Gα15 protein having at least 70 % sequence homology to SEQ. ID. NO. 2,

b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene,

wherein said cell stably expresses said Gα15 protein at sufficient levels to permit promiscuous coupling to said GPCR, and wherein said second heterologous promoter is directly or indirectly modulated by the activity of said Gα15 protein,

- ii) contacting said cell with a test chemical; and
iii) detecting a change in reporter gene expression by comparing reporter gene expression prior to addition of said test chemical with reporter gene expression after addition of said test chemical.

95. The method of claim 94 wherein said cell comprises a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR.

96. The method of claim 94, wherein said GPCR is not naturally expressed in said cell.

97. The method of claim 94, wherein said detecting comprises fluorescence detection.

98. The method of claim 94, further comprising contacting said cell with a reporter gene substrate.

99. The method of claim 94, further comprising contacting said cell with a compound that increases calcium levels inside said cell.

100. The method of claim 99, wherein said compound is selected from the group consisting of ionomycin and thapsigargin.

101. The method of claim 94, further comprising contacting said cell with phorbol myristate acetate or an analog thereof.

- 68
102. (Amended) A method of functionally profiling a test chemical comprising the steps of.
- i) contacting a panel of cells with a test chemical, said panel of cells comprising, a plurality of cell clones, each cell clone comprising
 - a) a GPCR,
 - b) a first heterologous promoter operably linked to a first polynucleotide encoding a G α 15 protein having at least 70 % sequence homology to SEQ. ID. NO. 2,
 - c) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene,wherein said cell stably expresses said G α 15 protein at sufficient levels to permit promiscuous coupling to said GPCR, wherein said second heterologous promoter is directly or indirectly modulated by the activity of said G α 15 protein, and wherein each cell clone differs only with respect to the GPCR that is expressed,
 - ii) contacting said cell clones with a test chemical;
 - iii) detecting reporter gene expression from said cell clones
 - iv) comparing reporter gene expression between said cell clones.

103. The method of claim 102 wherein said cell clone comprises a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR.

104. The method of claim 102, wherein said GPCR is not naturally expressed in said cell.

105. The method of claim 102, wherein said detecting comprises fluorescence detection.

- Sub D12*
106. The method of claim 102, further comprising contacting said cell with a reporter gene substrate.
107. The method of claim 102, further comprising contacting said cell with a compound that increases calcium levels inside said cell.
108. The method of claim 107, wherein said compound is selected from the group consisting of ionomycin and thapsigargin.
109. The method of claim 107, further comprising contacting said cell with phorbol myristate acetate or an analog thereof.

Please add new claims as below.

- Sub D13*
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- 110. The method of claim 63, wherein said G α 15 protein has at least 80 % sequence homology to SEQ. ID. NO. 2.
111. The method of claim 71, wherein said G α 15 protein has at least 80 % sequence homology to SEQ. ID. NO. 2.
112. The method of claim 73, wherein said G α 15 protein has at least 80 % sequence homology to SEQ. ID. NO. 2.
113. The method of claim 81, wherein said G α 15 protein has at least 80 % sequence homology to SEQ. ID. NO. 2.
114. The method of claim 90, wherein said G α 15 protein has at least 80 % sequence homology to SEQ. ID. NO. 2.

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115. The method of claim 94, wherein said Gα15 protein has at least 80 % sequence homology to SEQ. ID. NO. 2.
116. The method of claim 102, wherein said Gα15 protein has at least 80 % sequence homology to SEQ. ID. NO. 2.
117. The method of claim 63, wherein said Gα15 protein has at least 95 % sequence homology to SEQ. ID. NO. 2.
118. The method of claim 71, wherein said Gα15 protein has at least 95 % sequence homology to SEQ. ID. NO. 2.
119. The method of claim 75, wherein said Gα15 protein has at least 95 % sequence homology to SEQ. ID. NO. 2.
120. The method of claim 81, wherein said Gα15 protein has at least 95 % sequence homology to SEQ. ID. NO. 2.
121. The method of claim 90, wherein said Gα15 protein has at least 95 % sequence homology to SEQ. ID. NO. 2.
122. The method of claim 94, wherein said Gα15 protein has at least 95 % sequence homology to SEQ. ID. NO. 2.
123. The method of claim 102, wherein said Gα15 protein has at least 95 % sequence homology to SEQ. ID. NO. 2.—